UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/820,099	03/27/2001	Jan G.J. van de Winkel	MXI-170	2545

59819 7590 07/11/2006

LAHIVE & COCKFIELD, LLP
MEDAREX, INC.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
BLANCHARD, DAVID J	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 07/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/820,099	VAN DE WINKEL, JAN G.J.	
	Examiner	Art Unit	
	David J. Blanchard	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*..

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-12 and 25-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-12 and 25-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 2-5 and 13-24 are cancelled.

Claims 1 and 6 have been amended.

Claims 25-33 have been added.

2. Claims 1, 6-12 and 25-33 are pending and under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. This Office Action contains New Grounds of Rejections.

Response to Arguments

5. The rejection of claims 1, 6, 8 and 11-12 under 35 U.S.C. 102(b) as being anticipated by Mannhalter et al (U.S. Patent 5,808,000, issued 9/15/1998) is maintained.

The response filed 4/20/2006 argues that claim 1 has been amended to specify that monomeric IgA or the portion thereof that binds FcαRI is linked to the agent. This has been fully considered but is not found persuasive. Claim 1 as amended only requires monomeric IgA to be linked by chemical conjugation or recombinant genetic fusion, not the "portion thereof that binds to FcαRI". Thus, the claim still reads on the administration of monomeric IgA, which comprises the Fc region that binds to FcαRI (i.e., portion of monomeric IgA that binds FcαRI) linked to the antigen-binding antibody fragment (i.e., "an agent", particularly in view of claim 6) and the art of Mannhalter et al still applies. Applicant is advised that even if the claim recited that the portion of

monomeric IgA that binds to FcαRI linked to an agent by chemical conjugation or recombinant genetic fusion, the art of Mannhalter et al would still apply since monomeric IgA assembly occurs by genetic recombination of immunoglobulin genes *in vivo*, which is merely one interpretation of recombinant genetic fusion.

Thus, Mannhalter et al anticipate the claims.

6. The rejection of claims 1, 6, 8-11 and applied to newly added claims 26-27 and 29-32 under 35 U.S.C. 102(b) as being anticipated by van Spriel et al (Journal of Infectious Diseases, 179(3):661-669, first publicly available date of 3/3/1999) as evidenced by Van Egmond et al (Nature Medicine, 6(6):68-685, June 2000, IDS reference F2 filed 1/22/02) is maintained.

The response filed 4/20/2006 states that the claims are drawn to methods which encompass the use of monomeric IgA or a portion of monomeric IgA which binds to FcαRI linked to an agent. The response argues that applicant is not claiming any anti-FcαRI binding portion but a specific molecule, which is not taught by the cited reference. Applicant points out that van Spriel et al do not teach using monomeric IgA or a portion of monomeric IgA. This has been fully considered but is not found persuasive. The examiner agrees that van Spriel et al do not teach monomeric IgA, however, the claims recite that the administered complex comprises monomeric IgA or portion thereof that binds FcαRI, which broadly reads on an anti-FcαRI Fab linked to a *C. albicans* directed F(ab')2 as taught in the prior art. A portion of monomeric IgA that binds to FcαRI broadly embraces Fab fragments that bind to FcαRI, since a Fab fragment is a "portion"

of monomeric IgA. Applicant is reminded that the isotypic determinants or heavy chain antigenic determinants unique to IgA are found in the constant regions, not the Fab portion. Applicant has not provided any evidence showing that the prior art Fab fragment does not necessarily possess the characteristics of a Fab fragment of monomeric IgA. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

Thus, van Spriel et al anticipate the claims as evidenced by Van Egmond et al.

7. The rejection of claims 1, 6-12 and applied to newly added claims 26-33 are rejected under 35 U.S.C. 102(e) as being anticipated by Deo et al (US Patent 5,922,845, filed 7/11/1996) as evidenced by Van Egmond et al (Nature Medicine, 6(6):68-685, June 2000, Ids reference F2 filed 1/22/02) is maintained.

The response filed 4/20/2006 argues that like van Spriel et al above, Deo et al do not teach monomeric IgA, or the use of monomeric IgA. The examiner agrees that Deo et al do not teach monomeric IgA, however, as discussed above the claims recite that the administered complex comprises monomeric IgA or portion thereof that binds FcαRI, which broadly reads on the administration of an antigen-binding antibody fragment (i.e., Fab, Fab', $F(ab')_2$, Fv or single-chain Fv) that binds FcαRI linked to an antibody or antigen-binding fragment thereof (i.e., "an agent") that binds a bacteria, virus, fungi or cancer cell as taught by Deo et al. A portion of monomeric IgA that binds to FcαRI broadly embraces antigen-binding antibody fragments that bind to FcαRI, since an antigen-binding antibody fragment is a "portion" of monomeric IgA. Again, the isotypic determinants or heavy chain antigenic determinants unique to IgA are found in

the constant regions, not the antigen-binding portion of the antibody. Applicant has not provided any evidence showing that the prior art antigen-binding antibody fragment does not necessarily possess the characteristics of the antigen-binding antibody fragment (i.e., portion) of monomeric IgA. *In re Best*, 562 F.2d at 1255, 195 USPQ at 433.

New Grounds of Objections/Rejections

Specification

8. The amendment to the specification filed 4/1/2003 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The amendment claims priority to U.S. Provisional Application No. 60/192,727, filed March 27, 2001, which is incorporated by reference in its entirety. The priority application cannot be incorporated by reference after the original filing of the instant application. This objection can be overcome by removing the incorporation by reference statement.

See United States Patent and Trademark Office OG Notices: 1268 OG 89 (18 March 2003) "Benefit of Prior-Filed Application" (see Part VII).

Applicant is required to cancel the new matter in the reply to this Office Action

9. The Shen et al citation at pg. 18, line 26 of the specification contains the incorrect page range. The correct page range is pp. 4117-4122. Additionally, the term "Fc$\alpha\alpha$RI" at pg. 19, line 20 should be corrected to "FcαRI". The specification has not been

checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Appropriate correction is required.

19. Claims 1, 6-12 and 25-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The response filed 4/20/2006 has introduced NEW MATTER into the claims. Claim 1 as presently amended recites a method of removing a target cell or antigen from the circulatory system of a subject comprising administering monomeric IgA or a portion thereof that binds to FcαRI, linked to an agent which specifically binds the target cell or antigen, wherein monomeric IgA and the agent are linked by chemical conjugation or recombinant genetic fusion. Newly added claims 25-26 recite said method comprising administering monomeric IgA linked to an agent which specifically binds the target cell or antigen (claim 25) or administering monomeric IgA or a portion thereof that binds to FcαRI, linked to a non-FcαRI binding agent which specifically binds the target cell or antigen. The response points to pg. 2, lines 35-37, pg. 8, lines 22-24 and pg. 13, lines 1-4 of the as filed specification for support. Upon review of the as filed disclosure, the specification discloses a molecular complex comprising a first portion,

which specifically binds FcαRI expressed on liver Kupffer cell or which specifically binds monomeric IgA or the Fc region thereof linked to a second portion that specifically binds the target cell or antigen and wherein the first and second portions are linked by chemical conjugation or by genetic fusion (see also as filed claims; 3/27/2001). The disclosure of a first portion that targets FcαRI or monomeric IgA or the Fc region thereof does not provide adequate written support for a first portion of the molecular complex that is monomeric IgA or portion thereof that binds to FcαRI as presently claimed. There is insufficient guidance and direction to the currently claimed features. For example, pg. 2, lines 33-35 and pg. 8, lines 20-22 of the as filed specification disclose "the first portion of the complex binds a site on the FcαR that is distinct from the binding site for IgA, so that binding of the complex is not blocked by endogenous IgA and "it is likely that serum IgA (up to 4.0mg/ml) may interfere with the activity of IgA mAbs under physiological conditions." (pg. 9, lines 7-9). Based on the as filed disclosure which criticizes and discourages the use of monomeric IgA or portion thereof that binds FcαRI, one of ordinary skill in the art would not have been led to the claimed method of administering a complex comprising monomeric IgA or portion thereof that binds FcαRI linked via chemical conjugation or recombinant genetic fusion to an agent that specifically binds the target cell or antigen in view that serum IgA may interfere with the activity of such a complex under physiological conditions and the disclosure of using a complex that binds a site on the FcαR that is distinct from the binding site for IgA, so that binding of the complex is not blocked by endogenous IgA. The Federal Circuit has pointed out that under United States law, a description that does not render a claimed

invention obvious cannot sufficiently describe the invention for the purposes of the written description requirement of 35 U.S.C. 112. See MPEP 2163(I)(A).

Additionally, there are no working examples of the claimed method wherein administration of monomeric IgA or a portion thereof that binds to FcαRI is linked to an agent that binds a target cell or antigen, thereby eliminating the target cell or antigen from the circulatory system of a subject, i.e., the claimed method has not been reduced to practice. The examiner acknowledges that proof of reduction to practice is not necessary in every case, however, reduction to practice is strong evidence of completion and hence, possession under the first paragraph of 35 U.S.C. 112. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. As presently amended and newly presented, the claims now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in the present claims in the specification or claims, as filed, or remove these limitations from the claims in response to this Office Action.

Conclusion

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached at (571) 272-0832. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827

SHEELA HUFF
PRIMARY EXAMINER